

Beyond the Science: Navigating Today's Drug Development Climate

Turning Uncertainty Towards a Prescription for Future NMD Breakthroughs

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Lumanity tracks drug development for >500 NMDs

However, few have approved therapies, and drug development efforts remain underinvested

NMDs are diverse in pathophysiology, genetic and acquired

- Central and peripheral nervous system
- Neuromuscular junctions
- Muscle structure
- Motor-nerve cells in the spinal cord

- Metabolism
- Inflammation
- Senescence



NEUROMUSCULAR DISORDERS

Muscular Dystrophies	Metabolic Myopathies	Motor Neuron Diseases	Mitochondrial Disorders	Peripheral nerve Diseases	NM Junction Diseases	Autoimmune & Inflammatory (AIID)	Associated with Aging
DMD,BMD,LGM, FSHD, DM, OPMD	Pompe's Disease FAOD Carnitine Deficiency	ALS, SMA, SBMA	Friedreich Ataxia, MELAS	Charcot-Marie Tooth, Giant Axonal Neuropathy	LEMS, congenital Myasthenic Syndrome	Inclusion Body Myositis, CIDP, MG	Sarcopenia Neurodegeneration

NMDs have been a fertile proving ground for Novel Modalities

First approvals: Exon Skipping ODNs, Splice Modifiers, AAV Gene Therapy, FcRn…

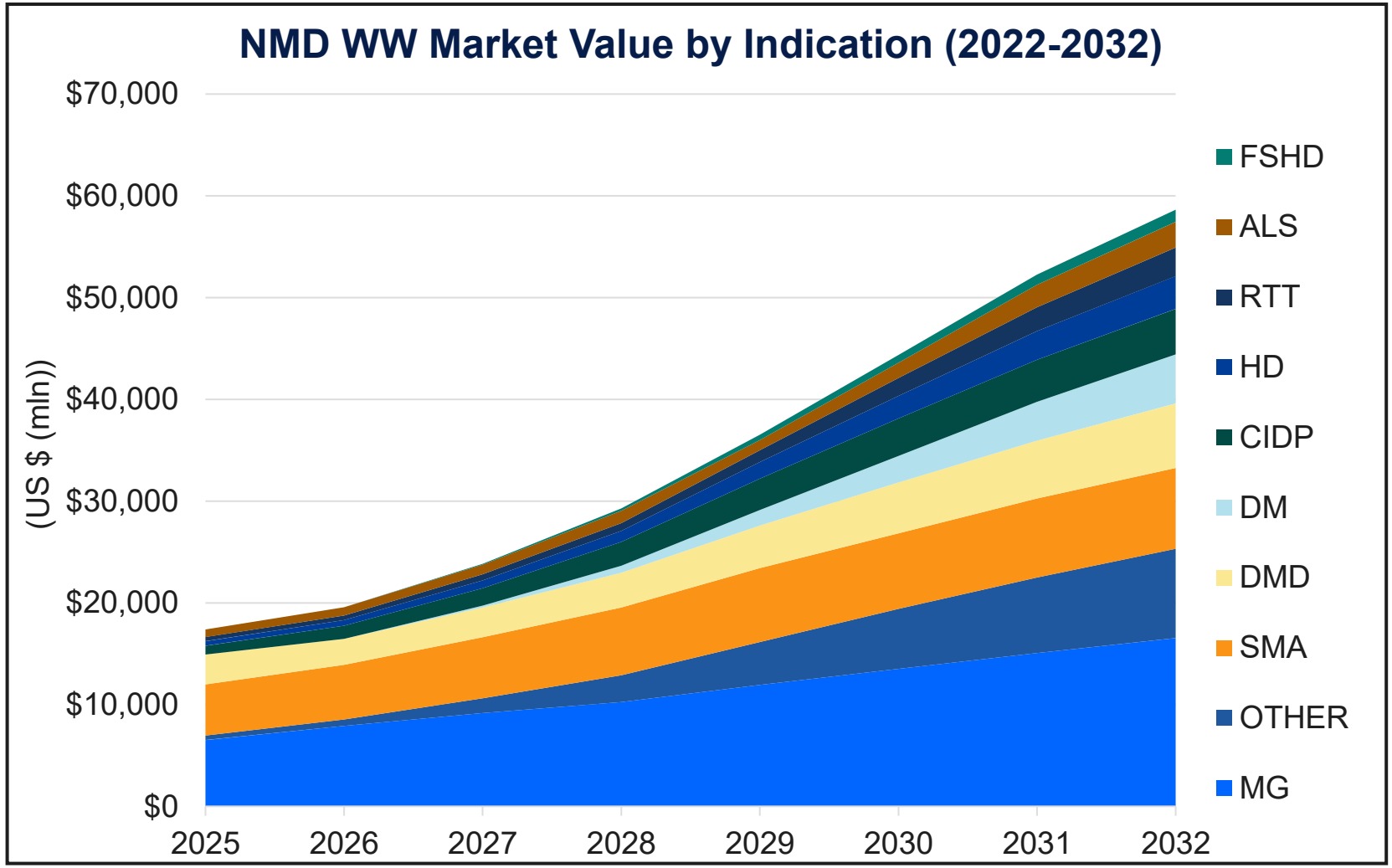
Small Molecules	Peptides and Protein Therapeutics	Antibodies	Nucleic Acids	Gene Correction and Augmentation	Cell Therapy and Regenerative Med
Drug delivery, formulation and enabling platforms: technology (non-viral and viral) improvements in biodistribution, PK and PD, and devices					

▪ Immune Modulators
▪ Inhibitors
▪ Chaperones
▪ Substrate reduction
▪ Transcription, Translation enhancers, Splicing
▪ Epigenetics
▪ Protein degraders
▪ Mitochondrial bioenergetics and mitophagy
▪ Macrocycles
▪ Radionuclides
▪ radiosensitizers
	▪ Plasma/tissue derived proteins (Ig, albumin, AAT, hemostasis, etc.)
	▪ Recombinant Proteins
	  ▪ Clotting factors
	  ▪ Cytokines
	  ▪ Hormones
	  ▪ Growth factors
	▪ Peptides
	▪ Enzyme Replacement
		▪ Plasma Polyclonal Igs
		▪ Monoclonal antibodies
		▪ mAB fragments
		▪ Scaffolds
		▪ Darpins
		▪ Intrabodies
		▪ Diabodies
		▪ Bispecific mABs
		▪ Bispecific T-Cell Engagers
		▪ ADCs
		▪ Radioimmunotherapy
			▪ Immune Modulator
			▪ Antisense
			▪ Splice/Exon modifiers
			▪ RNAi (siRNA and others)
			▪ Translational Readthrough
			▪ µRNA
			▪ mRNA
			▪ Circular RNA
			▪ Aptamers / Ribozyme
			▪ RNA Base Editing
			▪ tRNA
				▪ Viral vectors
				  ▪ Retro/Lentiviral
				  ▪ AdV, AAV
				▪ Non-viral
				  ▪ Plasmids /
				  ▪ Fragments
				  ▪ Transposons
				▪ Gene editing with Meganucleases
				  ▪ Zinc Fingers
				  ▪ TALENS
				  ▪ CRISPR/Cas9
				▪ DNA Base Editing
				▪ Prime Editing
				▪ Designer Recombinases
					▪ Organ/Tissue replacement
					▪ Autologous / allogeneic cell therapy
					▪ Other cells:
					  ▪ e.g. ES, iPS
					▪ Mitochondrial transfer
					▪ Devices
					  ▪ Encapsulation
					  ▪ Scaffolds
					  ▪ Implants
					  ▪ Micro-organs
					  ▪ Aphaeresis

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Rapid growth of NMD Market projected – Largely driven by MG, SMA, DMD and small contributions across many Ultra-Rare Disorders

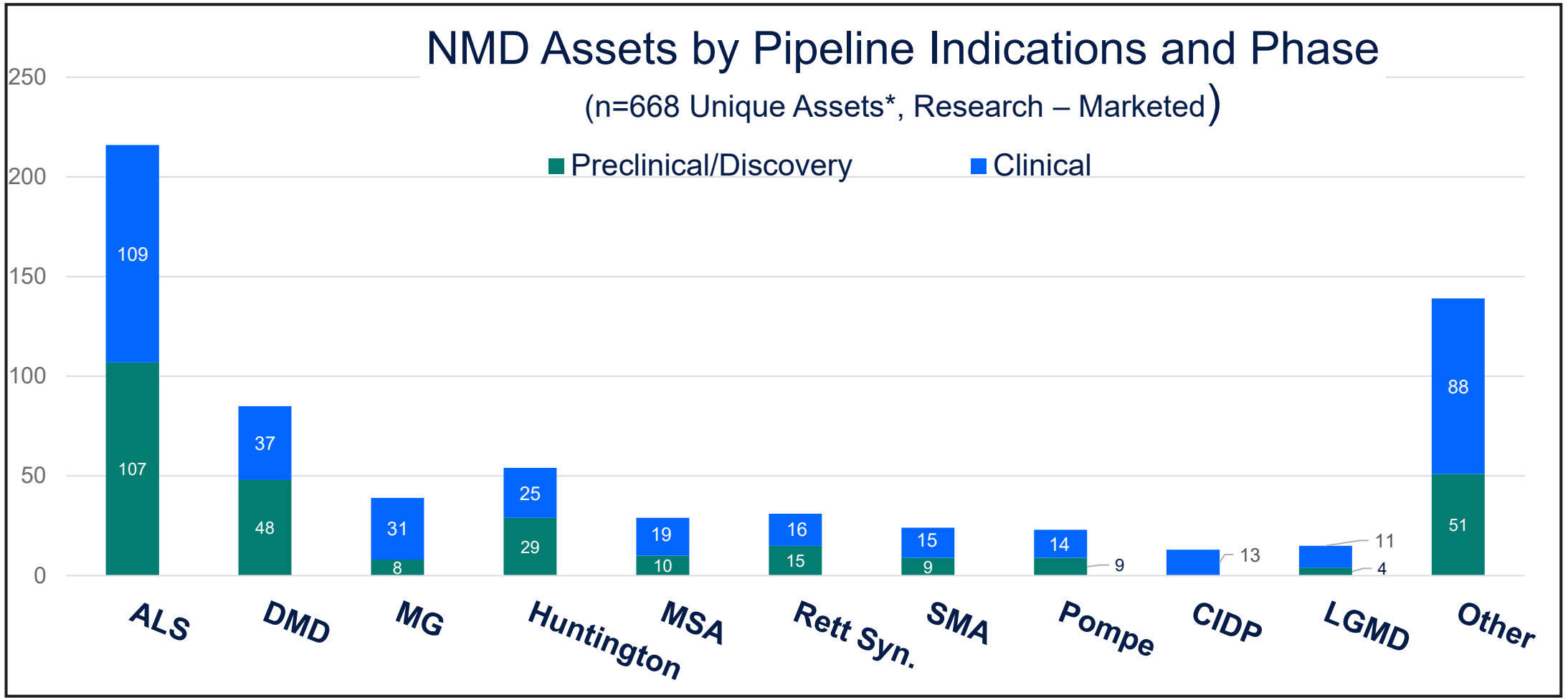
Top Assets Driving Indication Sales	
Vyvgart argenx (MG) Biologic (FcRN Ab)	$3.3B (2025) $5.6B (2032)
Elevidys Sarepta & Roche (DMD) Gene Therapy	$1.3M (2025) $925M (2032)
Evrysdi Roche (SMA) SMN2 Small Molecule	$2.2B (2025) $3.1B (2032)
Ultomiris Astrazeneca (MG) Anti-C5 mAb	$1.9B (2025) $3.4B (2032)
Spinraza Biogen (SMA) Antisense oligonucleotide	$1.6B (2025) $1.2B (2032)
Zolgensma Novartis (SMA) Gene Therapy	$1.2B (2025) $2.0B (2032)
Radicava Mitsubushi Chemical (ALS) Antioxidant	$685M (2025) $98M (2032)



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Evaluate Pharma
FSHD – Facioscapulohumeral Muscular Dystrophy, ALS – Amyotrophic Lateral Sclerosis, RTT – Rett Syndrome, HD – Huntington's Disease, DM – Myotonic Dystrophy, DMD – Duchenne's Muscular Dystrophy, SMA – Spinal Muscular Atrophy, MG – Myasthenia Gravis
*Complete list of "Other" Indications: Peripheral Neuropathy, Limb Girdle Muscular Dystrophy, Polymyositis, Dermatomyositis, Hemolytic Anemia, Spinocerebellar Ataxia, Friedrich's Ataxia, Mitochondrial Disease

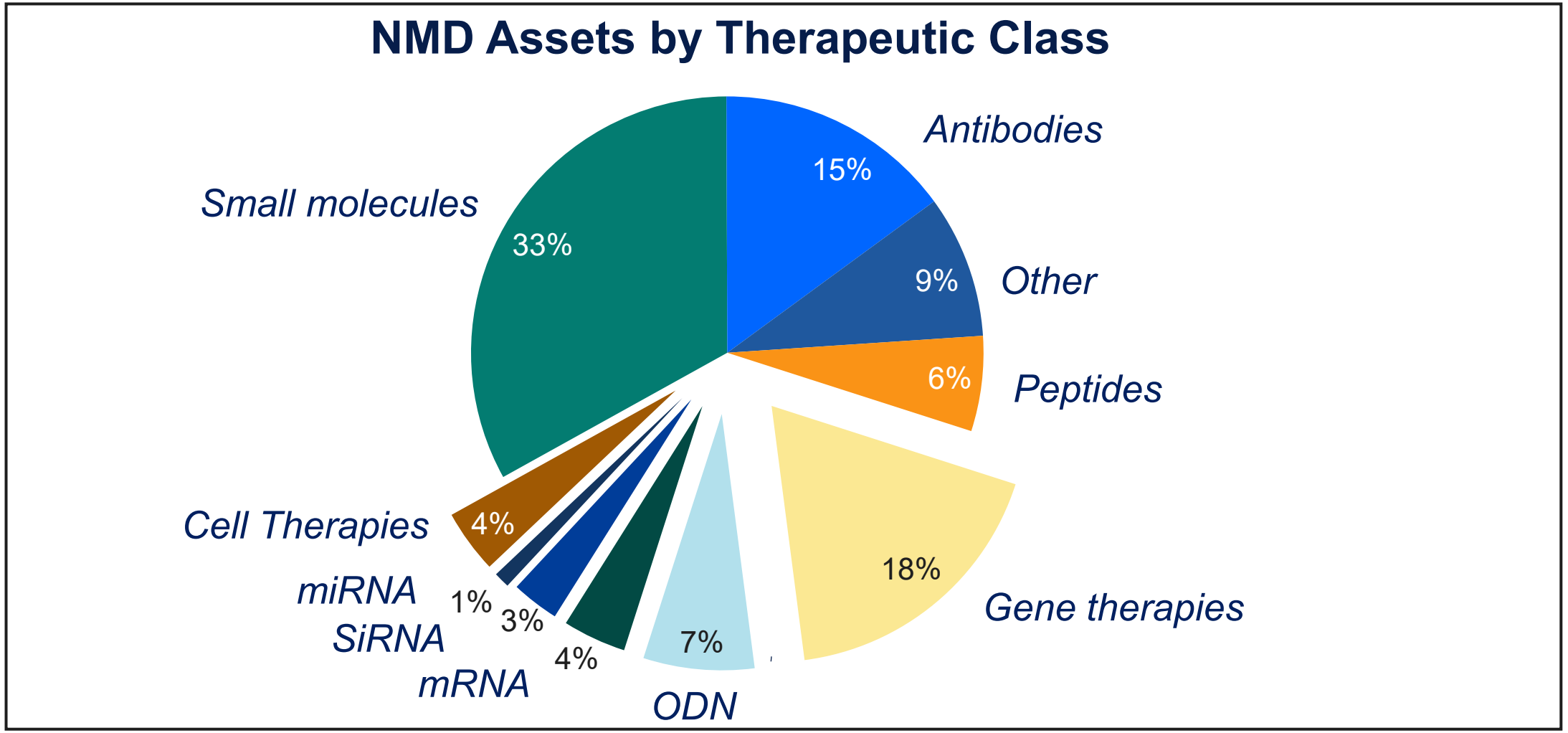
However, R&D still focused on small set of NMDs – Highly active in more prevalent populations lacking Disease Modifiers



AdisInsights, GlobalData
Note: Products that are Registered or Pre-registered are included in Clinical group.
Assets are represented more than once if developed for multiple indications
Note: 9.43% of assets originated in China.
ALS – Amyotrophic Lateral Sclerosis, CIDP – Chronic Inflammatory Demyelinating Polyradiculoneuropathy, LGMD – Limb Girdle Muscular Dystrophy
*Complete list of "Other" Indications: Charcot-Marie-Tooth Disease, Mitochondrial Myopathies, Dermatomyositis, Myotonic Dystrophy, Facioscapulohumeral Muscular Dystrophy, Ataxia (including Friedrich's Ataxia), Autoimmune Hemolytic Anemia, Polymyositis, Inclusion Body Myositis

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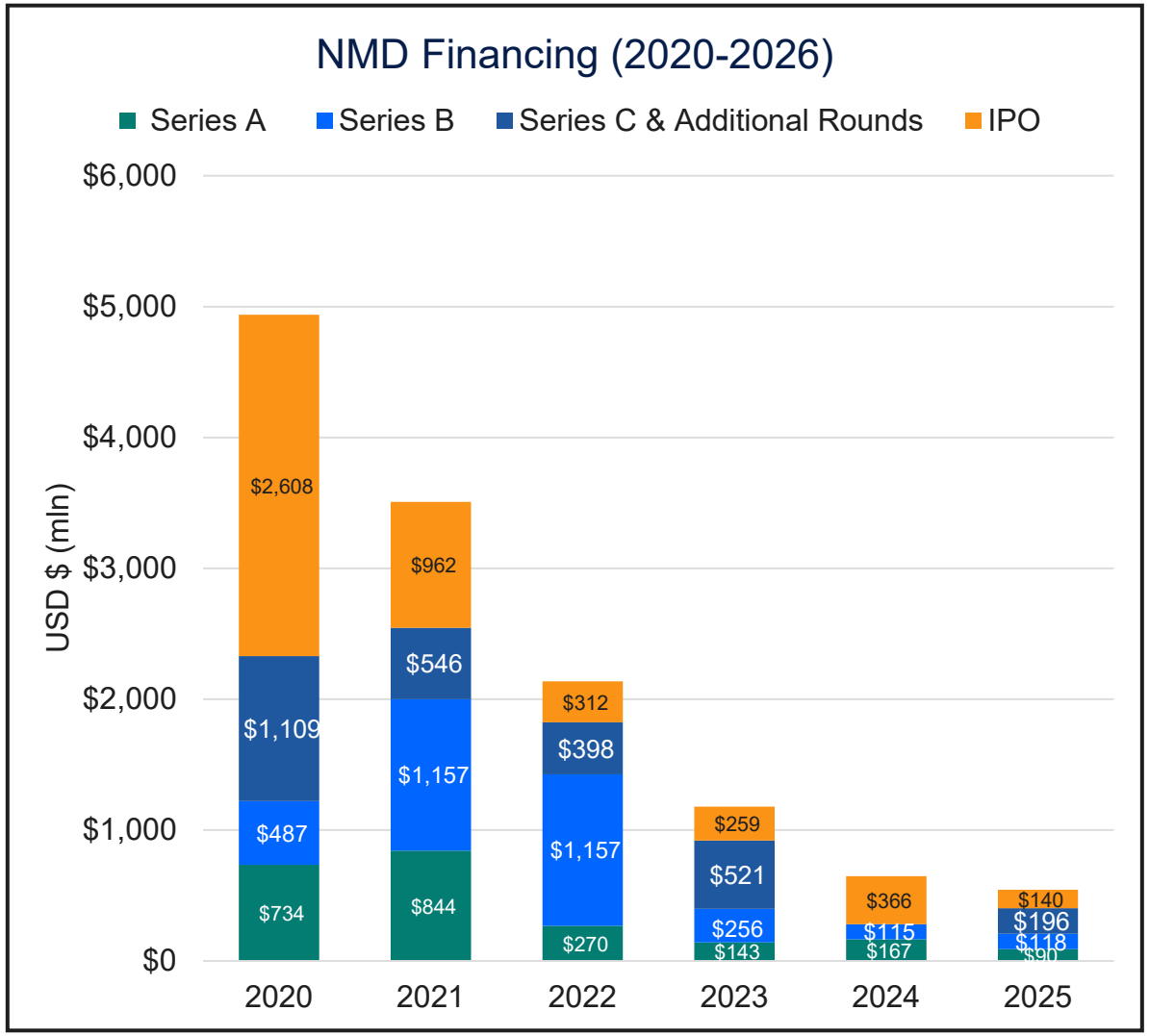
A third of all assets in development for NMDs are Advanced Therapies



AdisInsights, GlobalData; Note: Products that are Registered or Pre-registered are included in Clinical group; Assets are represented more than once if developed for multiple indications
RNA – Ribonucleic Acid, siRNA – Small interfering RNA, miRNA – Micro RNA
*Complete list of "Other" Class: Exosome Therapies, Stem Cell Therapies, Sulfones, Heavy Metals, Serpins, Fv Fragments, Enzymes, Peptide hydrolase, Vaccine, Stilbenes, Thiosulfates, Sugar Alcohols, Sulfonamides, Diagnostic Agents, Antigens, Gangliosides, Oxidoreductase, Vitamins, Thiazoles, Acetonitrile, Sulfides, Peptidomimetics, Urea Compounds, Propionates, Bacteria, Endopeptidases, Ester, Triazoles, Flavonoid, Analgesics, T-lymphocyte Cell Therapies, Unsaturated Fatty Acid, Hexoamines, Amines, Isoxazoles, Polyethylene Glycols, Phenyl Ethers

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VC funding has decreased to less than 20% of peak 2020 levels – Follow-on placements and IPO market at low point



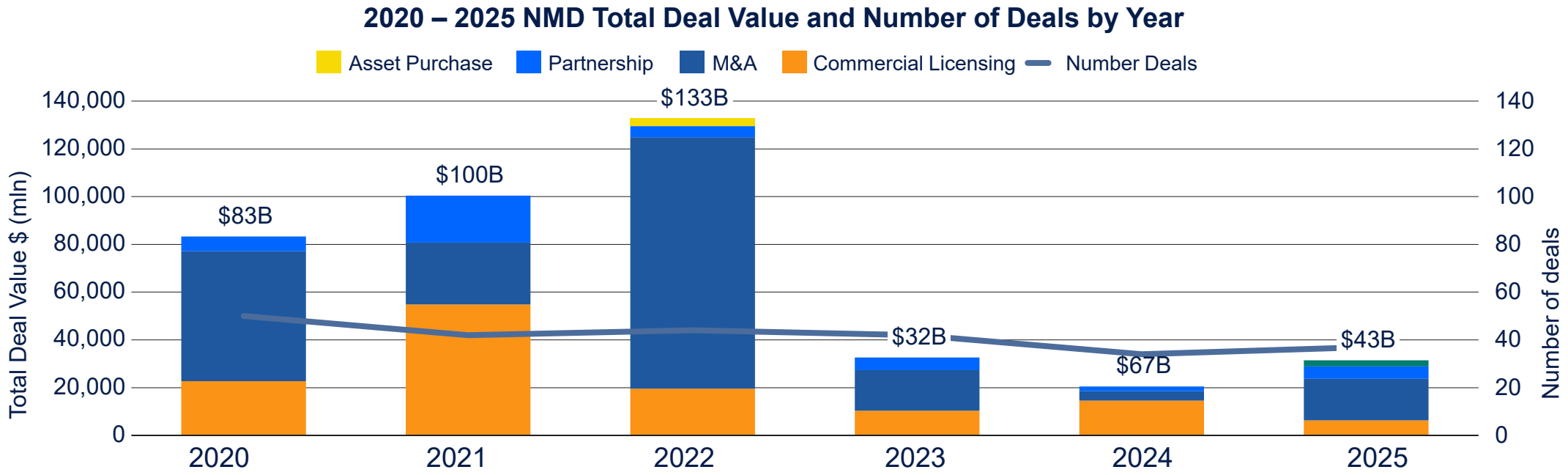
VC Series A Financing Rounds for NMD Therapies		
Company	**Value**	**Date Completed**
Vectory Therapeutics	$147,541,672	November 2023
Cour Pharmaceuticals Development	$105,000,000	January 2024
Loqus23 Therapeutics	$35,055,068	October 2024
Coave Therapeutics	$33,831,331	January 2025
Teitur Trophics ApS	$32,222,190	March 2025
Alchemab Therapeutics	$32,000,000	September 2025
Axoltis Pharma	$24,262,049	December 2025
Actimed Therapeutics	$16,214,705	August 203
Argo Biopharma	$5,602,841	November 2023

IPOs for NMD Therapies		
Company	**Value**	**Date Completed**
Kyverna Therapeutics	$366,850,000	February 2024
Neumora Therapeutics	$250,070,000	September 2023
Maze Therapeutics	$140,000,000	January 2025

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BCIQ
2026 YTD Financing: $34 mln in Series B

Pharma deal number has been down substantially as interest in GTx wanes; however, deal value can be high for innovators with quality data



Key Deals from 2024-2025

AVIDITY BIOSCIENCES, NOVARTIS	$12B	
MITSUBISHI CHEMICAL GROUP, BainCapital PRIVATE EQUITY	$3.6B	
Tanabe Pharma, SHIONOGI	$2.5B	
KATE THERAPEUTICS, NOVARTIS	$1.1B	
arrowhead pharmaceuticals, SAREPTA THERAPEUTICS	$9.15B	
PTC THERAPEUTICS, NOVARTIS	$2.9B	
voyager therapeutics, NOVARTIS	$1.3B	
Lilly, Juvena THERAPEUTICS	$650M	
RemeGen, VOR	$4.13B	
LONGBOARD PHARMACEUTICALS, Lundbeck	$2.6B	
VectorY THERAPEUTICS, SHAPE THERAPEUTICS	$1.2B	
astria THERAPEUTICS, biocryst	$765M	

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BCIQ, 2026 YTD Financing: 1 deal; $205 mln total value

Selective financing and partnerships due to regulatory uncertainty and clinical/commercial setbacks – Despite progress in innovation



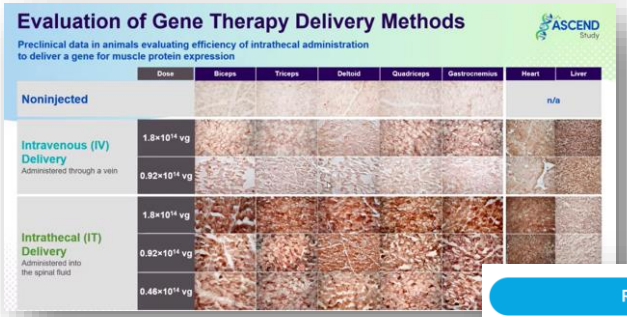
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Innovation Perseveres:
Building on 1st Gen to improve Product Profiles

Improving micro dystrophin

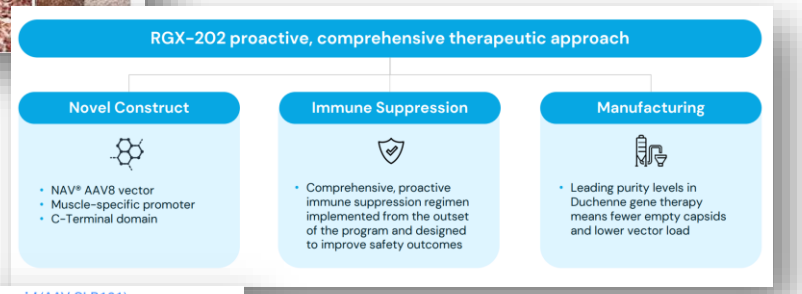
insmed

- IT Administration



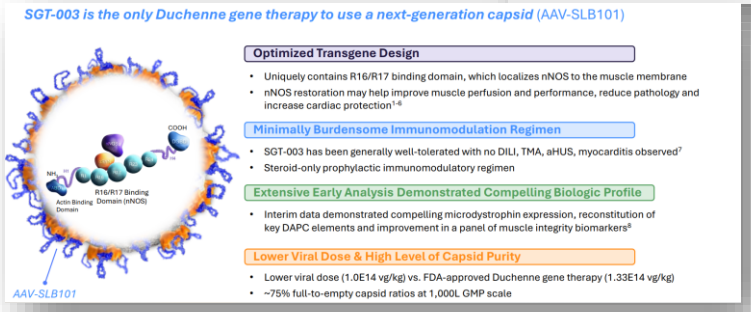
REGENXBIO

- Optimized Transgene & IST



SOLID BIOSCIENCES

- Myotropic Vector & Optimized Transgene



Delivering Mid and Full-length Dystrophin

Viral Delivery Strategies:

- Multi-AAV vector approaches to overcome insert CDS size limitations:
  - RNA End Joining
  - Split Intein
  - Gene editing

Non-Viral Delivery Strategies:

- LNP and nanoparticle delivery
- mRNA
- Gene and RNA editing

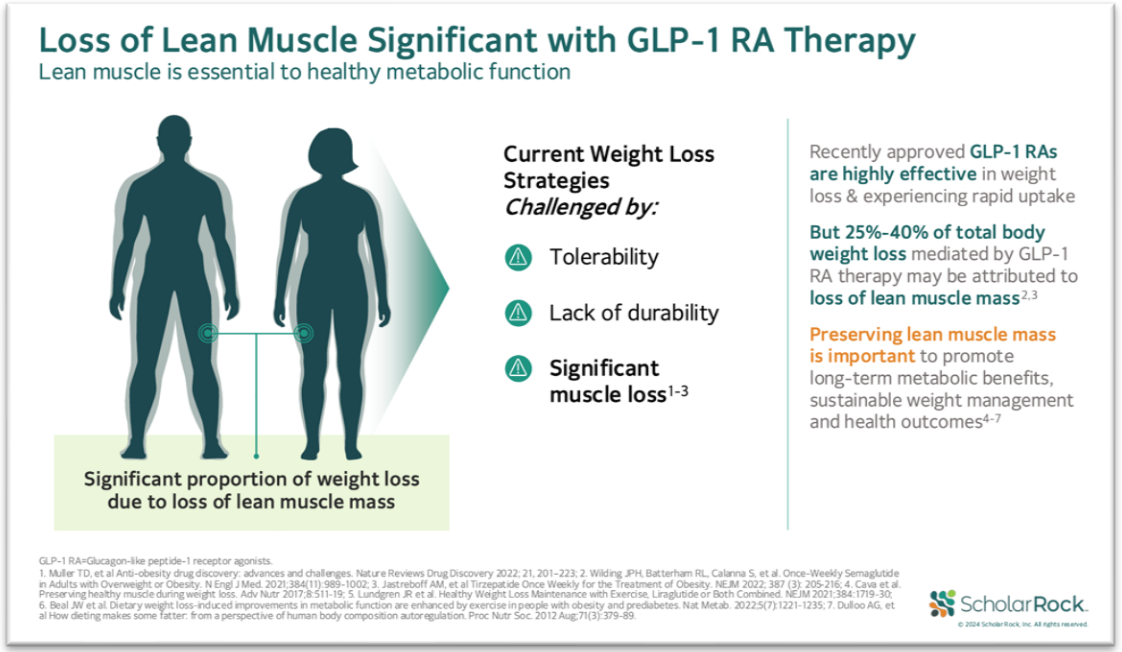
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https://www.youtube.com/watch?v=qHeyw3dvVnY; https://investors.solidbio.com/static-files/2566f07f-215d-40ff-9edb-874aefee6239; https://ir.regenxbio.com/static-files/a7f4f464-cba3-412b-88b1-02de8bf70faf

Pharma's focus on prevalent diseases is dragging on NMD capital, but may soon accelerate Disease Modifying drugs for rarer disorders

Obesity market prompted pharma and biotech to search for drugs to limit muscle loss
R&D funding for Obesity may drive discovery of agents with activity in NMDs

- Investors saw data on **SRRK's promyostatin** inhibitor in **SMA** as derisking broader potential in **Obesity**
- **Lilly** acquired **Versanis** for **$1.9B** for bimagrumab for Obesity – However, terminated mid-stage trial recently.
- **Juvena** entered a **$650M** collaboration to identify candidates that improve muscle health
- **Roche** paid **$2.7B** to acquire **Carmot** and sees potential for its **anti-myostatin antibody** in Obesity.
- **Regeneron** is advancing two muscle-sparing antibodies in **combination with incretin-based drugs**
- **AstraZeneca** paid **$170M** up front to acquire **SixPeaks Bio,** for muscle sparing weight-loss drugs



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BCIQ, Endpoint News, Fierce Biotech, BioSpace, https://investors.scholarrock.com/

Enter CAR T-Cells for NMDs: Will they provide durable remissions for Autoimmune & Inflammatory Myopathies?

7 CAR T-cell therapies have been approved in oncology:

1. **Kymriah** *(r/r ALL; 3L DLBCL; 3L FL)*
2. **Yescarta** *(3L DLBCL; r/r FL; 2L DLBCL)*
3. **Tecartus** *(2L MCL; r/r ALL)*
4. **Breyanzi** *(3L DLBCL; 2L DLBCL; 3L CLL; 3L FL; 3L MCL)*
5. **Abecma** *(5L MM; 3L MM)*
6. **Carvykti** *(5L MM; 2L MM)*
7. **Aucatzyl** *(ALL)*

CAR T-cell therapies in autoimmune:

- Meaningful competition is emerging across autoimmune indications with assets in late-stage development

Pipeline

Asset	SPS	MG	MS	SLE/LN	SSc	Other[a]
KYV-101	✓	✓	✓	✓	✓	
Descartes-08		✓	✓	✓		
CABA-201		✓		✓	✓	✓
BMS-986353		✓	✓	✓	✓	✓
ADI-001	✓			✓	✓	✓
FT819				✓	✓	✓
CTX112				✓	✓	✓
YTB-323				✓	✓	✓
Anito-cell		✓				
Obe-cell				✓		
SC291				✓		
AZD0120				✓		
LMY-920				✓		
SYNCAR-001/ STK-009				✓		
SBT777101						✓
Azer-cel						✓

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ALL, acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HM, hematologic malignancies; MCL, mantle cell lymphoma; Mel, metastatic melanoma; MG, myasthenia gravis; MM, multiple myeloma; r/r, relapsed/refractory; SPS, stiff person syndrome; SS, synovial sarcoma.
[a]Assets may be targeting additional indications (eg, idiopathic inflammatory myopathies) or their trial is unspecified.
Sources: ClinicalTrials.gov; Company Websites.

NMD Investing and R&D Takeaways

- Today's $16B NMD Market is on nearly a 20% CAGR growth trajectory to $60B by 2033
- NMD sector drives innovation of novel drug mechanisms and modalities through collaboration between Patient Advocates, Academic Investigators and Industry
- R&D Investment and NMD Pipeline still leave many underserved patent populations
- Tight capital markets and regulatory uncertainty has impacted pace of early innovation
- Some first-generation gene therapies have demonstrated less than stellar TPPs increasing commercial risk, even when reaching the market.
- Private financings and IPOs at a low point while Pharma Partnerships and acquisitions are beginning to increase since last year
- However, deals have been selective for programs with quality data to justify value and potential to overcome commercial risks.
- Next gen therapeutic modalities promise to improve clinical benefits and commercial potential.

Thank you

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